

REMARKS

Reconsideration and re-examination are respectfully requested. After entering these amendments, claims 1-35 and 48-50 will be pending.

Claims 36-47 and 51 have been canceled as being drawn to the non-elected invention(s), and claims 2, 3, 12, 13, 19, 20, 27, 28, and 31 have been amended to remove subject matter directed to the non-elected invention(s). A marked-up version of these amendments is found beginning on a separate sheet entitled "Version With Markings to Show Changes Made." No new matter is believed to be added.

Provisional Obviousness-Type Double Patenting Rejections

Claims 1-35 and 48-50 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-36 and 56-139 of copending Application No. 09/465,300. It is believed that the provisional rejection is improper but, nonetheless, Applicants will further address the rejection, if maintained, upon withdrawal of all other rejections.

Claims 1-35 and 48-50 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-40, 54, and 55 of copending Application No. 09/466,582. It is believed that the provisional rejection is improper but, nonetheless, Applicants will further address the rejection, if maintained, upon withdrawal of all other rejections.

Claims 1-35 and 48-50 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7, 11-13, and 17-35 of copending Application No. 09/599,364. It is believed that the provisional rejection is improper but, nonetheless, Applicants will further address the rejection, if maintained, upon withdrawal of all other rejections.

Claims 1, 2, 11-15, 19-21, 23, 25, 27-29, 31-35, and 48-50 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 12-14, 20-23, 25, 27-29, 31, 39, 46, and 48 of copending Application No. 09/281,209. It is believed that the provisional rejection is improper but, nonetheless, Applicants will further address the rejection, if maintained, upon withdrawal of all other rejections.

Claims 1-5, 7, 11-13, and 48 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 58-65 of copending Application No. 09/948,807. It is believed that the provisional rejection is improper but, nonetheless, Applicants will further address the rejection, if maintained, upon withdrawal of all other rejections.

Rejection Under 35 U.S.C. 103

Claims 1, 2, 11-15, 17, 19-23, 25, 27, 28, 31-35, 48, and 49 were rejected as being unpatentable over Palladino et al. (U.S. Patent No. 5,780,426). That rejection is respectfully traversed.

The Office Action (page 7, third paragraph) acknowledges that Palladino et al. does not disclose a specific species having all of the components as set forth in Applicants' independent claims 1 and 11. The Office takes the position, however, that it would have been obvious to one of ordinary skill at the time the invention was made to generate a compound and uses thereof as claimed by the Applicants because Palladino et al. disclose that each component, as claimed by Applicants, may be present in Palladino et al.'s composition.

It is respectfully submitted that it would not be obvious to one of skill in the art to modify the teaching of Palladino et al. so as to arrive at Applicants' invention of claims 1, 2, 11-15, 17, 19-23, 25, 27, 28, 31-35, 48, and 49. Moreover, Applicants submit that the Office has not established a *prima facie* case of obviousness. Specifically, the Office has not provided some suggestion or motivation, either in the reference itself or in the knowledge generally available to one of ordinary skill in the art, to modify Palladino et al. as suggested. MPEP 2143. For example, Applicants' composition of claim 1 comprises, *inter alia*, a targeting moiety and a chelator, wherein the targeting moiety is bound to the chelator. By contrast, Palladino et al. teaches at column 16, line 66 that their peptide can include a chelator for use as a penetration enhancer. There is no teaching or suggestion in Palladino et al. of a compound comprising a targeting moiety and a chelator, wherein the targeting moiety is bound to the chelator, as recited in Applicants' claim 1. It is respectfully submitted that the Office has not provided some suggestion or motivation to modify the teaching of Palladino et al. to achieve the compound of claim 1 or composition of claim 11, nor the subject matter encompassed by the cited claims depending from claim 1 or 11. Withdrawal of the rejection is requested.

Specification

The disclosure was objected to for not containing a heading entitled "Brief Description of the Drawings" and a description of the drawings. It is believed that the application does not contain drawings and, hence, that a Brief Description of the Drawings is not required. Withdrawal of the objection is requested.

Return of Notice of Draftsperson's Patent Drawing Review for Application No. 09/688,947

Enclosed herewith is the Notice of Draftsperson's Patent Drawing Review for Application No. 09/688,947 which was erroneously mailed with the Office Action for the present application.

Application No.: 09/281,474
Attorney Docket No.: DM-6958

CONCLUSION

In view of the foregoing amendments and remarks, allowance of the above-referenced application is respectfully requested. The Examiner is invited to contact the undersigned if there are any questions concerning the prosecution of this application.

The Commissioner is authorized to charge Deposit Account 19-3880 (Bristol-Myers Squibb Company) for any requisite fees due or to credit any overpayment.

Respectfully submitted,



Date: 10/18/02

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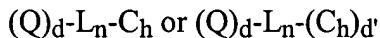
VERSION WITH MARKINGS TO SHOW CHANGES MADE

In showing the changes, deleted material is shown surrounded by brackets and added material is shown by underlining.

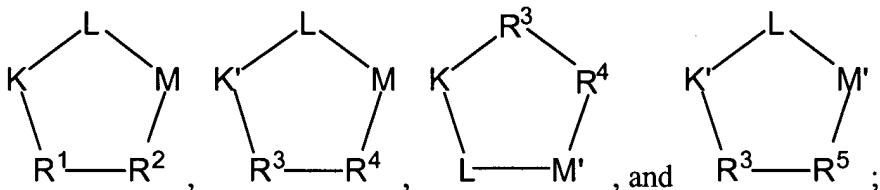
IN THE CLAIMS:

2. (Amended) A compound according to Claim 1, wherein the targeting moiety is a peptide or a mimetic thereof and the receptor is [selected from the group: EGFR, FGFR, PDGFR, Flk-1/KDR, Flt-1, Tek, Tie, neuropilin-1, endoglin, endosialin, Axl,] $\alpha_v\beta_3$ [, $\alpha_v\beta_5$, $\alpha_5\beta_1$, $\alpha_4\beta_1$, $\alpha_1\beta_1$, and $\alpha_2\beta_2$] and the linking group is present between the targeting moiety and chelator.

3. (Amended) A compound according to Claim 2, [the receptor is the integrin $\alpha_v\beta_3$ and] the compound is of the formula:



wherein, Q is a peptide independently selected from the group:



K is an L-amino acid independently selected at each occurrence from the group: arginine, citrulline, N-methylarginine, lysine, homolysine, 2-aminoethylcysteine, δ -N-2-imidazolinylornithine, δ -N-benzylcarbamoylornithine, and β -2-benzimidazolylacetyl-1,2-diaminopropionic acid;

K' is a D-amino acid independently selected at each occurrence from the group: arginine, citrulline, N-methylarginine, lysine, homolysine, 2-aminoethylcysteine, δ -N-2-imidazolinylornithine, δ -N-benzylcarbamoylornithine, and β -2-benzimidazolylacetyl-1,2-diaminopropionic acid;

L is independently selected at each occurrence from the group: glycine, L-alanine, and D-alanine;

M is L-aspartic acid;

M' is D-aspartic acid;

R¹ is an amino acid substituted with 0-1 bonds to L_n, independently selected at each occurrence from the group: glycine, L-valine, D-valine, alanine, leucine, isoleucine, norleucine, 2-aminobutyric acid, 2-aminohexanoic acid, tyrosine, phenylalanine, thienylalanine, phenylglycine, cyclohexylalanine, homophenylalanine, 1-naphthylalanine, lysine, serine, ornithine, 1,2-diaminobutyric acid, 1,2-diaminopropionic acid, cysteine, penicillamine, and methionine;

R² is an amino acid, substituted with 0-1 bonds to L_n, independently selected at each occurrence from the group: glycine, valine, alanine, leucine, isoleucine, norleucine, 2-aminobutyric acid, 2-aminohexanoic acid, tyrosine, L-phenylalanine, D-phenylalanine, thienylalanine, phenylglycine, biphenylglycine, cyclohexylalanine, homophenylalanine, L-1-naphthylalanine, D-1-naphthylalanine, lysine, serine, ornithine, 1,2-diaminobutyric acid, 1,2-diaminopropionic acid, cysteine, penicillamine, methionine, and 2-aminothiazole-4-acetic acid;

R³ is an amino acid, substituted with 0-1 bonds to L_n, independently selected at each occurrence from the group: glycine, D-valine, D-alanine, D-leucine, D-isoleucine, D-norleucine, D-2-aminobutyric acid, D-2-aminohexanoic acid, D-tyrosine, D-phenylalanine, D-thienylalanine, D-phenylglycine, D-cyclohexylalanine, D-homophenylalanine, D-1-naphthylalanine, D-lysine, D-serine, D-ornithine, D-1,2-diaminobutyric acid, D-1,2-diaminopropionic acid, D-cysteine, D-penicillamine, and D-methionine;

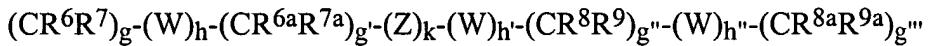
R⁴ is an amino acid, substituted with 0-1 bonds to L_n, independently selected at each occurrence from the group: glycine, D-valine, D-alanine, D-leucine, D-isoleucine, D-norleucine, D-2-aminobutyric acid, D-2-aminohexanoic acid, D-tyrosine, D-phenylalanine, D-thienylalanine, D-phenylglycine, D-cyclohexylalanine, D-homophenylalanine, D-1-naphthylalanine, D-lysine, D-serine, D-ornithine, D-1,2-diaminobutyric acid, D-1,2-diaminopropionic acid, D-cysteine, D-penicillamine, D-methionine, and 2-aminothiazole-4-acetic acid;

R^5 is an amino acid, substituted with 0-1 bonds to L_n , independently selected at each occurrence from the group: glycine, L-valine, L-alanine, L-leucine, L-isoleucine, L-norleucine, L-2-aminobutyric acid, L-2-aminohexanoic acid, L-tyrosine, L-phenylalanine, L-thienylalanine, L-phenylglycine, L-cyclohexylalanine, L-homophenylalanine, L-1-naphthylalanine, L-lysine, L-serine, L-ornithine, L-1,2-diaminobutyric acid, L-1,2-diaminopropionic acid, L-cysteine, L-penicillamine, L-methionine, and 2-aminothiazole-4-acetic acid;

provided that one of R^1 , R^2 , R^3 , R^4 , and R^5 in each Q is substituted with a bond to L_n , further provided that when R^2 is 2-aminothiazole-4-acetic acid, K is N-methylarginine, further provided that when R^4 is 2-aminothiazole-4-acetic acid, K and K' are N-methylarginine, and still further provided that when R^5 is 2-aminothiazole-4-acetic acid, K' is N-methylarginine;

d is selected from 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

L_n is a linking group having the formula:



provided that $g+h+g'+k+h'+g''+h''+g'''$ is other than 0;

W is independently selected at each occurrence from the group: O, S, NH, NHC(=O), C(=O)NH, C(=O), C(=O)O, OC(=O), NHC(=S)NH, NHC(=O)NH, SO₂, (OCH₂CH₂)_s, (CH₂CH₂O)_{s'}, (OCH₂CH₂CH₂)_{s''}, (CH₂CH₂CH₂O)_t, and (aa)_{t'};

aa is independently at each occurrence an amino acid;

Z is selected from the group: aryl substituted with 0-3 R^{10} , C₃₋₁₀ cycloalkyl substituted with 0-3 R^{10} , and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R^{10} ;

R^6 , R^{6a} , R^7 , R^{7a} , R^8 , R^{8a} , R^9 and R^{9a} are independently selected at each occurrence from the group: H, =O, COOH, SO₃H, PO₃H, C_{1-C5} alkyl substituted with 0-3 R^{10} , aryl substituted with 0-3 R^{10} , benzyl substituted with 0-3 R^{10} , and C_{1-C5} alkoxy substituted

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Attorney Docket No.: DM-6958

with 0-3 R¹⁰, NHC(=O)R¹¹, C(=O)NHR¹¹, NHC(=O)NHR¹¹, NHR¹¹, R¹¹, and a bond to C_h;

R¹⁰ is independently selected at each occurrence from the group: a bond to C_h, COOR¹¹, OH, NHR¹¹, SO₃H, PO₃H, aryl substituted with 0-3 R¹¹, C₁₋₅ alkyl substituted with 0-1 R¹², C₁₋₅ alkoxy substituted with 0-1 R¹², and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹¹;

R¹¹ is independently selected at each occurrence from the group: H, aryl substituted with 0-1 R¹², a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-1 R¹², C₃₋₁₀ cycloalkyl substituted with 0-1 R¹², polyalkylene glycol substituted with 0-1 R¹², carbohydrate substituted with 0-1 R¹², cyclodextrin substituted with 0-1 R¹², amino acid substituted with 0-1 R¹², polycarboxyalkyl substituted with 0-1 R¹², polyazaalkyl substituted with 0-1 R¹², peptide substituted with 0-1 R¹², wherein the peptide is comprised of 2-10 amino acids, and a bond to C_h;

R¹² is a bond to C_h;

k is selected from 0, 1, and 2;

h is selected from 0, 1, and 2;

h' is selected from 0, 1, 2, 3, 4, and 5;

h" is selected from 0, 1, 2, 3, 4, and 5;

g is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g" is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

g''' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

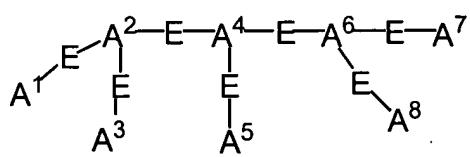
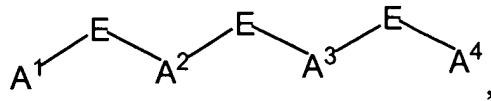
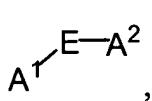
s' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

s" is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

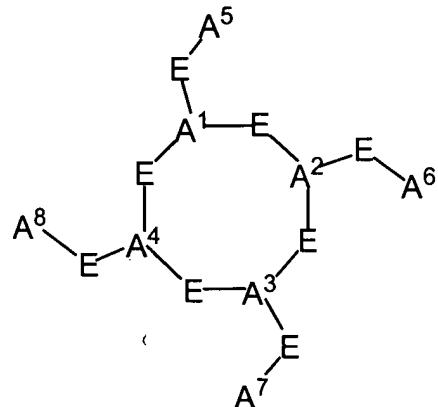
t is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

t' is selected from 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10;

C_h is a metal bonding unit having a formula selected from the group:



, and



;

$A^1, A^2, A^3, A^4, A^5, A^6, A^7$, and A^8 are independently selected at each occurrence from the group $N, NR^{13}, NR^{13}R^{14}, S, SH, S(Pg), O, OH, PR^{13}, PR^{13}R^{14}, P(O)R^{15}R^{16}$, and a bond to L_n ;

E is a bond, CH , or a spacer group independently selected at each occurrence from the group:

C_1-C_{10} alkyl substituted with 0-3 R^{17} , aryl substituted with 0-3 R^{17} , C_{3-10} cycloalkyl substituted with 0-3 R^{17} , heterocyclo- C_{1-10} alkyl substituted with 0-3 R^{17} , wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S , and O , C_{6-10} aryl- C_{1-10} alkyl substituted with 0-3 R^{17} , C_{1-10} alkyl- C_{6-10} aryl- substituted with 0-3 R^{17} , and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S , and O and substituted with 0-3 R^{17} ;

R^{13} , and R^{14} are each independently selected from the group: a bond to L_n , hydrogen, C_1-C_{10} alkyl substituted with 0-3 R^{17} , aryl substituted with 0-3 R^{17} , C_{1-10} cycloalkyl substituted with 0-3 R^{17} , heterocyclo- C_{1-10} alkyl substituted with 0-3 R^{17} , wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S , and O , C_{6-10} aryl- C_{1-10} alkyl substituted with 0-3 R^{17} , C_{1-10} alkyl- C_{6-10} aryl- substituted with 0-3 R^{17} , a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S , and O and substituted with 0-3 R^{17} , and an electron, provided that when one of R^{13} or R^{14} is an electron, then the other is also an electron;

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alternatively, R¹³ and R¹⁴ combine to form =C(R²⁰)(R²¹);

R¹⁵ and R¹⁶ are each independently selected from the group: a bond to L_n, -OH, C₁-C₁₀ alkyl substituted with 0-3 R¹⁷, C₁-C₁₀ alkyl substituted with 0-3 R¹⁷, aryl substituted with 0-3 R¹⁷, C₃₋₁₀ cycloalkyl substituted with 0-3 R¹⁷, heterocyclo-C₁₋₁₀ alkyl substituted with 0-3 R¹⁷, wherein the heterocyclo group is a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O, C₆₋₁₀ aryl-C₁₋₁₀ alkyl substituted with 0-3 R¹⁷, C₁₋₁₀ alkyl-C₆₋₁₀ aryl- substituted with 0-3 R¹⁷, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R¹⁷;

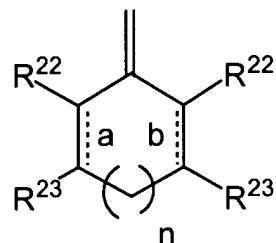
R¹⁷ is independently selected at each occurrence from the group: a bond to L_n, =O, F, Cl, Br, I, -CF₃, -CN, -CO₂R¹⁸, -C(=O)R¹⁸, -C(=O)N(R¹⁸)₂, -CHO, -CH₂OR¹⁸, -OC(=O)R¹⁸, -OC(=O)OR^{18a}, -OR¹⁸, -OC(=O)N(R¹⁸)₂, -NR¹⁹C(=O)R¹⁸, -NR¹⁹C(=O)OR^{18a}, -NR¹⁹C(=O)N(R¹⁸)₂, -NR¹⁹SO₂N(R¹⁸)₂, -NR¹⁹SO₂R^{18a}, -SO₃H, -SO₂R^{18a}, -SR¹⁸, -S(=O)R^{18a}, -SO₂N(R¹⁸)₂, -N(R¹⁸)₂, -NHC(=S)NHR¹⁸, =NOR¹⁸, NO₂, -C(=O)NHOR¹⁸, -C(=O)NHNR¹⁸R^{18a}, -OCH₂CO₂H, 2-(1-morpholino)ethoxy, C₁-C₅ alkyl, C₂-C₄ alkenyl, C₃-C₆ cycloalkyl, C₃-C₆ cycloalkylmethyl, C₂-C₆ alkoxyalkyl, aryl substituted with 0-2 R¹⁸, and a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O;

R¹⁸, R^{18a}, and R¹⁹ are independently selected at each occurrence from the group: a bond to L_n, H, C₁-C₆ alkyl, phenyl, benzyl, C₁-C₆ alkoxy, halide, nitro, cyano, and trifluoromethyl;

Pg is a thiol protecting group;

R²⁰ and R²¹ are independently selected from the group: H, C₁-C₁₀ alkyl, -CN, -CO₂R²⁵, -C(=O)R²⁵, -C(=O)N(R²⁵)₂, C₂-C₁₀ 1-alkene substituted with 0-3 R²³, C₂-C₁₀ 1-alkyne substituted with 0-3 R²³, aryl substituted with 0-3 R²³, unsaturated 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²³, and unsaturated C₃₋₁₀ carbocycle substituted with 0-3 R²³;

alternatively, R²⁰ and R²¹, taken together with the divalent carbon radical to which they are attached form:



R²² and R²³ are independently selected from the group: H, R²⁴, C₁-C₁₀ alkyl substituted with 0-3 R²⁴, C₂-C₁₀ alkenyl substituted with 0-3 R²⁴, C₂-C₁₀ alkynyl substituted with 0-3 R²⁴, aryl substituted with 0-3 R²⁴, a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O and substituted with 0-3 R²⁴, and C₃-C₁₀ carbocycle substituted with 0-3 R²⁴;

alternatively, R²², R²³ taken together form a fused aromatic or a 5-10 membered heterocyclic ring system containing 1-4 heteroatoms independently selected from N, S, and O;

a and **b** indicate the positions of optional double bonds and **n** is 0 or 1;

R²⁴ is independently selected at each occurrence from the group: =O, F, Cl, Br, I, -CF₃, -CN, -CO₂R²⁵, -C(=O)R²⁵, -C(=O)N(R²⁵)₂, -N(R²⁵)₃⁺, -CH₂OR²⁵, -OC(=O)R²⁵, -OC(=O)OR^{25a}, -OR²⁵, -OC(=O)N(R²⁵)₂, -NR²⁶C(=O)R²⁵, -NR²⁶C(=O)OR^{25a}, -NR²⁶C(=O)N(R²⁵)₂, -NR²⁶SO₂N(R²⁵)₂, -NR²⁶SO₂R^{25a}, -SO₃H, -SO₂R^{25a}, -SR²⁵, -S(=O)R^{25a}, -SO₂N(R²⁵)₂, -N(R²⁵)₂, =NOR²⁵, -C(=O)NHOR²⁵, -OCH₂CO₂H, and 2-(1-morpholino)ethoxy; and,

R²⁵, R^{25a}, and R²⁶ are each independently selected at each occurrence from the group: hydrogen and C₁-C₆ alkyl;

and a pharmaceutically acceptable salt thereof.

12. (Amended) A composition according to Claim 11, wherein the metallopharmaceutical is a diagnostic radiopharmaceutical, the metal is a radioisotope selected from the group: ^{99m}Tc, ⁹⁵Tc, ¹¹¹In, ⁶²Cu, ⁶⁴Cu, ⁶⁷Ga, and ⁶⁸Ga, the targeting moiety is a peptide or a mimetic thereof [and the receptor is selected from the group: EGFR, FGFR,

PDGFR, Flk-1/KDR, Flt-1, Tek, Tie, neuropilin-1, endoglin, endosialin, Axl, $\alpha_v\beta_3$, $\alpha_v\beta_5$, $\alpha_5\beta_1$, $\alpha_4\beta_1$, $\alpha_1\beta_1$, and $\alpha_2\beta_2$] and the linking group is present between the targeting moiety and chelator.

13. (Amended) A composition according to Claim 12, wherein the targeting moiety is a cyclic pentapeptide [and the receptor is $\alpha_v\beta_3$].

19. (Amended) A composition according to Claim 11, wherein the metallopharmaceutical is a therapeutic radiopharmaceutical, the metal is a radioisotope selected from the group: ^{186}Re , ^{188}Re , ^{153}Sm , ^{166}Ho , ^{177}Lu , ^{149}Pm , ^{90}Y , ^{212}Bi , ^{103}Pd , ^{109}Pd , ^{159}Gd , ^{140}La , ^{198}Au , ^{199}Au , ^{169}Yb , ^{175}Yb , ^{165}Dy , ^{166}Dy , ^{67}Cu , ^{105}Rh , ^{111}Ag , and ^{192}Ir , the targeting moiety is a peptide or a mimetic thereof [and the receptor is selected from the group: EGFR, FGFR, PDGFR, Flk-1/KDR, Flt-1, Tek, Tie, neuropilin-1, endoglin, endosialin, Axl, $\alpha_v\beta_3$, $\alpha_v\beta_5$, $\alpha_5\beta_1$, $\alpha_4\beta_1$, $\alpha_1\beta_1$, and $\alpha_2\beta_2$] and the linking group is present between the targeting moiety and chelator.

20. (Amended) A composition according to Claim 19, wherein the targeting moiety is a cyclic pentapeptide [and the receptor is $\alpha_v\beta_3$].

27. (Amended) A composition according to Claim 11, wherein the metallopharmaceutical is a MRI contrast agent, the metal is a paramagnetic metal ion selected from the group: Gd(III), Dy(III), Fe(III), and Mn(II), the targeting moiety is a peptide or a mimetic thereof [and the receptor is selected from the group: EGFR, FGFR, PDGFR, Flk-1/KDR, Flt-1, Tek, Tie, neuropilin-1, endoglin, endosialin, Axl, $\alpha_v\beta_3$, $\alpha_v\beta_5$, $\alpha_5\beta_1$, $\alpha_4\beta_1$, $\alpha_1\beta_1$, and $\alpha_2\beta_2$] and the linking group is present between the targeting moiety and chelator.

28. (Amended) A composition according to Claim 27, wherein the targeting moiety is a cyclic pentapeptide [and the receptor is $\alpha_v\beta_3$].

31. (Amended) A composition according to Claim 11, wherein the metallopharmaceutical is a X-ray contrast agent, the metal is selected from the group: Re, Sm, Ho, Lu, Pm, Y, Bi, Pd, Gd, La, Au, Au, Yb, Dy, Cu, Rh, Ag, and Ir, the targeting moiety is a cyclic pentapeptide, [the receptor is $\alpha_v\beta_3$,] and the linking group is present between the targeting moiety and chelator.